

212583.ST25  
SEQUENCE LISTING

<110> Nickoloff, Brian  
Miele, Lucio

<120> METHOD AND REAGENTS FOR EPITHELIAL BARRIER FORMATION AND TREATMENT  
OF MALIGNANT AND BENIGN SKIN DISORDERS BY MODULATING THE NOTCH PATHWAY

<130> 212583

<140> Unassigned

<141> 2001-08-31

<150> US 60/229,614

<151> 2000-08-31

<160> 18

<170> PatentIn version 3.1

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<211> 7332

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<213> Artificial Sequence

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<223> n is "a," "t," "g," or "c"

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Lys	Asn	Cys	Thr	Gln	Ser	Leu	Gln	Cys	Trp	Lys	Tyr	Phe	Ser	Asp	
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ggc	cac	tgt	gac	agc	cag	tgc	aac	tca	gcc	ggc	tgc	ctc	ttc	gac	4554
Gly	His	Cys	Asp	Ser	Gln	Cys	Asn	Ser	Ala	Gly	Cys	Leu	Phe	Asp	
1505		1510				1510					1515				
ggc	ttt	gac	tgc	cag	cgt	gcg	gaa	ggc	cag	tgc	aac	ccc	ctg	tac	4599
Gly	Phe	Asp	Cys	Gln	Arg	Ala	Glu	Gly	Gln	Cys	Asn	Pro	Leu	Tyr	
1520		1525				1525					1530				

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gac	cag	tac	tgc	aag	gac	cac	ttc	agc	gac	ggg	cac	tgc	gac	cag	4644
Asp	Gln	Tyr	Cys	Lys	Asp	His	Phe	Ser	Asp	Gly	His	Cys	Asp	Gln	
1535					1540						1545				
ggc	tgc	aac	agc	gcg	gag	tgc	gag	tgg	gac	ggg	ctg	gac	tgt	gcg	4689
Gly	Cys						Glu	Trp	Asp	Gly	Leu	Asp	Cys	Ala	
1550					1555						1560				
gag	cat	gta	ccc	gag	agg	ctg	gcg	gcc	ggc	acg	ctg	gtg	gtg	gtg	4734
Glu	His	Val	Pro	Glu	Arg	Leu	Ala	Ala	Gly	Thr	Leu	Val	Val	Val	
1565					1570						1575				
gtg	ctg	atg	ccg	ccg	gag	cag	ctg	cgc	aac	agc	tcc	ttc	cac	ttc	4779
Val	Leu		Met	Pro	Pro	Glu	Gln	Leu	Arg	Asn	Ser	Ser	Phe	His	Phe
1580					1585						1590				
ctg	cgg	gag	ctc	agc	cgc	gtg	ctg	cac	acc	aac	gtg	gtc	ttc	aag	4824
Leu	Arg	Glu	Leu	Ser	Arg	Val	Leu	His	Thr	Asn	Val	Val	Phe	Lys	
1595					1600						1605				
cgt	gac	gca	cac	ggc	cag	cag	atg	atc	ttc	ccc	tac	tac	ggc	cgc	4869
Arg	Asp	Ala	His	Gly	Gln	Gln	Met	Ile	Phe	Pro	Tyr	Tyr	Gly	Arg	
1610					1615						1620				
gag	gag	gag	ctg	cgc	aag	cac	ccc	atc	aag	cgt	gcc	gcc	gag	ggc	4914
Glu	Glu	Glu	Leu	Arg	Lys	His	Pro	Ile	Lys	Arg	Ala	Ala	Glu	Gly	
1625					1630						1635				
tgg	gcc	gca	cct	gac	gcc	ctg	ctg	ggc	cag	gtg	aag	gcc	tcg	ctg	4959
Trp	Ala	Ala	Pro	Asp	Ala	Leu	Leu	Gly	Gln	Val	Lys	Ala	Ser	Leu	
1640					1645						1650				
ctc	cct	ggt	ggc	agc	gag	ggt	ggg	cgg	cgg	cgg	agg	gag	ctg	gac	5004
Leu	Pro	Gly	Gly	Ser	Glu	Gly	Gly	Arg	Arg	Arg	Arg	Glu	Leu	Asp	
1655					1660						1665				
ccc	atg	gac	gtc	cgc	ggc	tcc	atc	gtc	tac	ctg	gag	att	gac	aac	5049
Pro	Met	Asp	Val	Arg	Gly	Ser	Ile	Val	Tyr	Leu	Glu	Ile	Asp	Asn	
1670					1675						1680				
cgg	cag	tgt	gtg	cag	gcc	tcc	tcg	cag	tgc	tcc	cag	agt	gcc	acc	5094
Arg	Gln	Cys	Val	Gln	Ala	Ser	Ser	Gln	Cys	Phe	Gln	Ser	Ala	Thr	
1685					1690						1695				
gat	gtg	gcc	gca	ttc	ctg	gga	gcg	ctc	gcc	tcg	ctg	ggc	agc	ctc	5139
Asp	Val	Ala	Ala	Phe	Leu	Gly	Ala	Leu	Ala	Ser	Leu	Gly	Ser	Leu	
1700					1705						1710				
aac	atc	ccc	tac	aag	atc	gag	gcc	gtg	cag	agt	gag	acc	gtg	gag	5184
Asn	Ile	Pro	Tyr	Lys	Ile	Glu	Ala	Val	Gln	Ser	Glu	Thr	Val	Glu	
1715					1720						1725				
ccg	ccc	ccg	ccg	gcg	cag	ctg	cac	ttc	atg	tac	gtg	gcg	gcg	gcc	5229
Pro	Pro	Pro	Pro	Ala	Gln	Leu	His	Phe	Met	Tyr	Val	Ala	Ala	Ala	
1730					1735						1740				
gcc	ttt	gtg	ctt	ctg	ttc	ttc	gtg	ggc	tgc	ggg	gtg	ctg	ctg	tcc	5274
Ala	Phe	Val	Leu	Leu	Phe	Phe	Val	Gly	Cys	Gly	Val	Leu	Leu	Ser	
1745					1750						1755				
cgc	aag	cgc	cgg	cng	cag	cat	ggc	cag	ctc	tgg	tcc	cct	gag	ggc	5319
Arg	Lys	Arg	Arg	Xaa	Gln	His	Gly	Gln	Leu	Trp	Phe	Pro	Glu	Gly	
1760					1765						1770				
ttc	aaa	gtg	tct	gag	gcc	agc	aag	aag	aag	cgg	cgg	gag	ncc	ctc	5364
Phe	Lys						Lys	Lys	Lys	Arg	Arg	Glu	Xaa	Leu	
1775					1780						1785				

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ggc	gag	gac	tcc	gtg	ggc	ctc	aag	ccc	ctg	aag	aac	gct	tca	gac	5409
Gly	Glu	Asp	Ser	Val	Gly	Leu	Lys	Pro	Leu	Lys	Asn	Ala	Ser	Asp	
1790					1795						1800				
ggt	gcc	ctc	atg	gac	gac	aac	cag	aat	gag	tgg	ggg	gac	gag	gac	5454
Gly	Ala	Leu	Met	Asp	Asp	Asn	Gln	Asn	Glu	Trp	Gly	Asp	Glu	Asp	
1805					1810						1815				
ctg	gag	acc	aag	aag	ttc	cg	ttc	gag	gag	ccc	gtg	gtt	ctg	cct	5499
Leu	Glu	Thr	Lys	Lys	Phe	Arg	Phe	Glu	Glu	Pro	Val	Val	Leu	Pro	
1820					1825						1830				
gac	ctg	gac	gac	cag	aca	gac	cac	cg	cag	tgg	act	cag	cag	cac	5544
Asp	Leu	Asp	Asp	Gln	Thr	Asp	His	Arg	Gln	Trp	Thr	Gln	Gln	His	
1835					1840						1845				
ctg	gat	gcc	gct	gac	ctg	cgc	atg	tct	gcc	atg	gcc	ccc	aca	ccg	5589
Leu	Asp	Ala	Ala	Asp	Leu	Arg	Met	Ser	Ala	Met	Ala	Pro	Thr	Pro	
1850					1855						1860				
ccc	cag	ggt	gag	gtt	gac	gcc	gac	tgc	atg	gac	gtc	aat	gtc	cgc	5634
Pro	Gln	Gly	Glu	Val	Asp	Ala	Asp	Cys	Met	Asp	Val	Asn	Val	Arg	
1865					1870						1875				
ggg	cct	gat	ggc	ttc	acc	ccg	ctc	atg	atc	gcc	tcc	tgc	agc	ggg	5679
Gly	Pro	Asp	Gly	Phe	Thr	Pro	Leu	Met	Ile	Ala	Ser	Cys	Ser	Gly	
1880					1885						1890				
ggc	ggc	ctg	gag	acg	ggc	aac	agc	gag	gaa	gag	gag	gac	gcg	ccg	5724
Gly	Gly	Leu	Glu	Thr	Gly	Asn	Ser	Glu	Glu	Glu	Glu	Asp	Ala	Pro	
1895					1900						1905				
gcc	gtc	atc	tcc	gac	ttc	atc	tac	cag	ggc	gcc	agc	ctg	cac	aac	5769
Ala	Val	Ile	Ser	Asp	Phe	Ile	Tyr	Gln	Gly	Ala	Ser	Leu	His	Asn	
1910					1915						1920				
cag	aca	gac	cgc	acg	ggc	gag	acc	gcc	ttg	cac	ctg	gcc	gcc	cgc	5814
Gln	Thr	Asp	Arg	Thr	Gly	Glu	Thr	Ala	Leu	His	Leu	Ala	Ala	Arg	
1925					1930						1935				
tac	tca	cgc	tct	gat	gcc	gcc	aag	cgc	ctg	ctg	gag	gcc	agc	gca	5859
Tyr	Ser	Arg	Ser	Asp	Ala	Ala	Lys	Arg	Leu	Leu	Glu	Ala	Ser	Ala	
1940					1945						1950				
gat	gcc	aac	atc	cag	gac	aac	atg	ggc	cgc	acc	ccg	ctg	cat	cg	5904
Asp	Ala	Asn	Ile	Gln	Asp	Asn	Met	Gly	Arg	Thr	Pro	Leu	His	Ala	
1955					1960						1965				
gct	gtg	tct	gcc	gac	gca	caa	ggt	gtc	ttc	cag	atc	ctg	atc	cgg	5949
Ala	Val	Ser	Ala	Asp	Ala	Gln	Gly	Val	Phe	Gln	Ile	Leu	Ile	Arg	
1970					1975						1980				
aac	cga	gcc	aca	gac	ctg	gat	gcc	cgc	atg	cat	gat	ggc	acg	acg	5994
Asn	Arg	Ala	Thr	Asp	Leu	Asp	Ala	Arg	Met	His	Asp	Gly	Thr	Thr	
1985					1990						1995				
cca	ctg	atc	ctg	gct	gcc	cgc	ctg	gcc	gtg	gag	ggc	atg	ctg	gag	6039
Pro	Leu	Ile	Leu	Ala	Ala	Arg	Leu	Ala	Val	Glu	Gly	Met	Leu	Glu	
2000					2005						2010				
gac	ctc	atc	aac	tca	cac	gcc	gac	gtc	aac	gcc	gta	gat	gac	ctg	6084
Asp	Leu	Ile	Asn	Ser	His	Ala	Asp	Val	Asn	Ala	Val	Asp	Asp	Leu	
2015					2020						2025				
ggc	aag	tcc	gcc	ctg	cac	tgg	gcc	gcc	gcc	gtg	aac	aat	gtg	gat	6129
Gly	Lys	Ser	Ala	Leu	His	Trp	Ala	Ala	Ala	Val	Asn	Asn	Val	Asp	
2030					2035						2040				

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gcc	gca	gtt	gtg	ctc	ctg	aag	aac	ggg	gct	aac	aaa	gat	atg	cag			
Ala	Ala	Val	Val	Leu	Leu	Lys	Asn	Gly	Ala	Asn	Lys	Asp	Met	Gln			
2045						2050					2055						
aac	aac	agg	gag	gag	aca	ccc	ctg	ttt	ctg	gcc	gcc	cgg	gag	ggc		6219	
Asn	Asn	Arg	Glu	Glu	Thr	Pro	Leu	Phe	Leu	Ala	Ala	Arg	Glu	Gly			
2060						2065					2070						
agc	tac	gag	acc	gcc	aag	gtg	ctg	ctg	gac	cac	ttt	gcc	aac	cgg		6264	
Ser	Tyr	Glu	Thr	Ala	Lys	Val	Leu	Leu	Asp	His	Phe	Ala	Asn	Arg			
2075						2080					2085						
gac	atc	acg	gat	cat	atg	gac	cgc	ctg	ccg	cgc	gac	atc	gca	cag		6309	
Asp	Ile	Thr	Asp	His	Met	Asp	Arg	Leu	Pro	Arg	Asp	Ile	Ala	Gln			
2090						2095					2100						
gag	cgc	atg	cat	cac	gac	atc	gtg	agg	ctg	ctg	gac	gag	tac	aac		6354	
Glu	Arg	Met	His	His	Asp	Ile	Val	Arg	Leu	Leu	Asp	Glut	Tyr	Asn			
2105						2110					2115						
ctg	gtg	cgc	agc	ccg	cag	ctg	cac	gga	gcc	ccg	ctg	ggg	ggc	acg		6399	
Leu	Val	Arg	Ser	Pro	Gln	Leu	His	Gly	Ala	Pro	Leu	Gly	Gly	Thr			
2120						2125					2130						
ccc	acc	ctg	tcg	ccc	ccg	ctc	tgc	tcg	ccc	aac	gac	tac	ctg	ggc		6444	
Pro	Thr	Leu	Ser	Pro	Pro	Leu	Cys	Ser	Pro	Asn	Gly	Tyr	Leu	Gly			
2135						2140					2145						
agc	ctc	aag	ccc	ggc	gtg	cag	ggc	aag	aag	gtc	cgc	aag	ccc	agc		6489	
Ser	Leu	Lys	Pro	Gly	Val	Gln	Gly	Lys	Lys	Val	Arg	Lys	Pro	Ser			
2150						2155					2160						
agc	aaa	ggc	ctg	gcc	tgt	gga	agc	aag	gag	gcc	aag	gac	ctc	aag		6534	
Ser	Lys	Gly	Leu	Ala	Cys	Gly	Ser	Lys	Glu	Ala	Lys	Asp	Leu	Lys			
2165						2170					2175						
gca	cgg	agg	aag	aag	tcc	cag	gay	ggc	aag	ggc	tgc	ctg	ctg	gac		6579	
Ala	Arg	Arg	Lys	Lys	Ser	Gln	Asp	Gly	Lys	Gly	Cys	Leu	Leu	Asp			
2180						2185					2190						
agc	tcc	ggc	atg	ctc	tcg	ccc	gtg	gac	tcc	ctg	gag	tca	ccc	cat		6624	
Ser	Ser	Gly	Met	Leu	Ser	Pro	Val	Asp	Ser	Leu	Glut	Ser	Pro	His			
2195						2200					2205						
ggc	tac	ctg	tca	gac	gtg	gcc	tgc	ccg	cca	ctg	ctg	ccc	tcc	ccg		6669	
Gly	Tyr	Leu	Ser	Asp	Val	Ala	Ser	Pro	Pro	Leu	Leu	Pro	Ser	Pro			
2210						2215					2220						
ttc	cag	cag	tct	ccg	tcc	gtg	ccc	ctc	aac	cac	ctg	cct	ggg	atg		6714	
Phe	Gln	Gln	Ser	Pro	Ser	Val	Pro	Leu	Asn	His	Leu	Pro	Gly	Met			
2225						2230					2235						
ccc	gac	acc	cac	ctg	ggc	atc	ggg	cac	ctg	aac	gtg	gcg	gcc	aag		6759	
Pro	Asp	Thr	His	Leu	Gly	Ile	Gly	His	Leu	Asn	Val	Ala	Ala	Lys			
2240						2245					2250						
ccc	gag	atg	gcg	gcf	ctg	ggt	ggg	ggc	ggc	cgg	ctg	gcc	ttt	gag		6804	
Pro	Glu	Met	Ala	Ala	Leu	Gly	Gly	Gly	Gly	Arg	Leu	Ala	Phe	Glu			
2255						2260					2265						
act	ggc	cca	cct	cgt	ctc	tcc	cac	ctg	cct	gtg	gcc	tct	ggc	acc		6849	
Thr	Gly	Pro	Pro	Arg	Leu	Ser	His	Leu	Pro	Val	Ala	Ser	Gly	Thr			
2270						2275					2280						
agc	acc	gtc	ctg	ggc	tcc	agc	agc	gga	ggg	gcc	ctg	aat	ttc	act		6894	
Ser	Thr	Val	Leu	Gly	Ser	Ser	Ser	Gly	Gly	Ala	Leu	Asn	Phe	Thr			
2285						2290					2295						

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gtg ggc ggg tcc acc agt ttg	aat ggt caa tgc gag	tgg ctg tcc	6939
Val Gly Gly Ser Thr Ser Leu	Asn Gly Gln Cys Glu	Trp Leu Ser	
2300 2305	2310		
cgg ctg cag agc ggc atg gtg	ccg aac caa tac aac	cct ctg cg	6984
Arg Leu Gln Ser Gly Met Val	Pro Asn Gln Tyr Asn	Pro Leu Arg	
2315 2320	2325		
ggg agt gtg gca cca ggc ccc	ctg agc aca cag gcc	ccc tcc ctg	7029
Gly Ser Val Ala Pro Gly Pro	Leu Ser Thr Gln Ala	Pro Ser Leu	
2330 2335	2340		
cag cat ggc atg gta ggc ccc	ctg cac agt agc ctt	gct gcc agc	7074
Gln His Gly Met Val Gly Pro	Leu His Ser Ser Leu	Ala Ala Ser	
2345 2350	2355		
gcc ctg tcc cag atg atg agc	tac cag ggc ctg ccc	agc acc cg	7119
Ala Leu Ser Gln Met Met Ser	Tyr Gln Gly Leu Pro	Ser Thr Arg	
2360 2365	2370		
ctg gcc acc cag cct cac ctg	gtg cag acc cag cag	gtg cag cca	7164
Leu Ala Thr Gln Pro His Leu	Val Gln Thr Gln Gln	Val Gln Pro	
2375 2380	2385		
caa aac tta cag atg cag cag	cag aac ctg cag cca	gca aac atc	7209
Gln Asn Leu Gln Met Gln Gln	Gln Asn Leu Gln Pro	Ala Asn Ile	
2390 2395	2400		
cag cag cag caa agc ctg cag	ccg cca cca cca cca	cca cag ccg	7254
Gln Gln Gln Ser Leu Gln	Pro Pro Pro Pro Pro	Pro Gln Pro	
2405 2410	2415		
cac ctt ggc gtg agc tca gca	gcc agc ggc cac ctg	ggc cg agc	7299
His Leu Gly Val Ser Ser Ala	Ala Ser Gly His Leu	Gly Arg Ser	
2420 2425	2430		
ttc ctg agt gga gag ccg agc	cag gca gac gtg		7332
Phe Leu Ser Gly Glu Pro Ser	Gln Ala Asp Val		
2435 2440			

<210> 2

<211> 2444

<212> PRT

<213> Artificial Sequence

<220>

<221> misc\_feature

<222> (891)..(891)

<223> The 'xaa' at location 891 stands for Gly, or Ala.

<220>

<221> misc\_feature

<222> (1763)..(1763)

<223> The 'xaa' at location 1763 stands for Gln, Arg, Pro, or Leu.

<220>

&lt;221&gt; misc\_feature

&lt;222&gt; (1787)..(1787)

&lt;223&gt; The 'Xaa' at location 1787 stands for Thr, Ala, Pro, or Ser.

&lt;220&gt;

&lt;223&gt; Constitutively Active Notch-1

&lt;400&gt; 2

Met	Pro	Pro	Leu	Leu	Ala	Pro	Leu	Leu	Cys	Leu	Ala	Leu	Leu	Pro	Ala
1				5					10					15	

Leu	Ala	Ala	Arg	Gly	Pro	Arg	Cys	Ser	Gln	Pro	Gly	Glu	Thr	Cys	Leu
			20				25					30			

Asn	Gly	Gly	Lys	Cys	Glu	Ala	Ala	Asn	Gly	Thr	Glu	Ala	Cys	Val	Cys
			35			40				45					

Gly	Gly	Ala	Phe	Val	Gly	Pro	Arg	Cys	Gln	Asp	Pro	Asn	Pro	Cys	Leu
			50			55				60					

Ser	Thr	Pro	Cys	Lys	Asn	Ala	Gly	Thr	Cys	His	Val	Val	Asp	Arg	Arg
65					70				75				80		

Gly	Val	Ala	Asp	Tyr	Ala	Cys	Ser	Cys	Ala	Leu	Gly	Phe	Ser	Gly	Pro
			85				90					95			

Leu	Cys	Leu	Thr	Pro	Leu	Asp	Asn	Ala	Cys	Leu	Thr	Asn	Pro	Cys	Arg
			100				105					110			

Asn	Gly	Gly	Thr	Cys	Asp	Leu	Leu	Thr	Leu	Thr	Glu	Tyr	Lys	Cys	Arg
			115			120				125					

Cys	Pro	Pro	Gly	Trp	Ser	Gly	Lys	Ser	Cys	Gln	Gln	Ala	Asp	Pro	Cys
	130				135					140					

Ala	Ser	Asn	Pro	Cys	Ala	Asn	Gly	Gly	Gln	Cys	Leu	Pro	Phe	Glu	Ala
145					150				155				160		

Ser	Tyr	Ile	Cys	His	Cys	Pro	Pro	Ser	Phe	His	Gly	Pro	Thr	Cys	Arg
	165					170					175				

Gln	Asp	Val	Asn	Glu	Cys	Gly	Gln	Lys	Pro	Arg	Leu	Cys	Arg	His	Gly
			180				185					190			

Gly	Thr	Cys	His	Asn	Glu	Val	Gly	Ser	Tyr	Arg	Cys	Val	Cys	Arg	Ala
	195					200					205				

Thr	His	Thr	Gly	Pro	Asn	Cys	Glu	Arg	Pro	Tyr	Val	Pro	Cys	Ser	Pro
	210				215					220					

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Ser Pro Cys Gln Asn Gly Gly Thr Cys Arg Pro Thr Gly Asp Val Thr  
225 230 235 240

His Glu Cys Ala Cys Leu Pro Gly Phe Thr Gly Gln Asn Cys Glu Glu  
245 250 255

Asn Ile Asp Asp Cys Pro Gly Asn Asn Cys Lys Asn Gly Gly Ala Cys  
260 265 270

Val Asp Gly Val Asn Thr Tyr Asn Cys Pro Cys Pro Pro Glu Trp Thr  
275 280 285

Gly Gln Tyr Cys Thr Glu Asp Val Asp Glu Cys Gln Leu Met Pro Asn  
290 295 300

Ala Cys Gln Asn Gly Gly Thr Cys His Asn Thr His Gly Gly Tyr Asn  
305 310 315 320

Cys Val Cys Val Asn Gly Trp Thr Gly Glu Asp Cys Ser Glu Asn Ile  
325 330 335

Asp Asp Cys Ala Ser Ala Ala Cys Phe His Gly Ala Thr Cys His Asp  
340 345 350

Arg Val Ala Ser Phe Tyr Cys Glu Cys Pro His Gly Arg Thr Gly Leu  
355 360 365

Leu Cys His Leu Asn Asp Ala Cys Ile Ser Asn Pro Cys Asn Glu Gly  
370 375 380

Ser Asn Cys Asp Thr Asn Pro Val Asn Gly Lys Ala Ile Cys Thr Cys  
385 390 395 400

Pro Ser Gly Tyr Thr Gly Pro Ala Cys Ser Gln Asp Val Asp Glu Cys  
405 410 415

Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn Thr  
420 425 430

Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Arg  
435 440 445

Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn Asp  
450 455 460

Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Met Cys Met Pro  
465 470 475 480

Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr Asp Glu Cys Ala Ser  
485 490 495

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Ser Pro Cys Leu His Asn Gly Arg Cys Leu Asp Lys Ile Asn Glu Phe  
500 505 510

Gln Cys Glu Cys Pro Thr Gly Phe Thr Gly His Leu Cys Gln Tyr Asp  
515 520 525

Val Asp Glu Cys Ala Ser Thr Pro Cys Lys Asn Gly Ala Lys Cys Leu  
530 535 540

Asp Gly Pro Asn Thr Tyr Thr Cys Val Cys Thr Glu Gly Tyr Thr Gly  
545 550 555 560

Thr His Cys Glu Val Asp Ile Asp Glu Cys Asp Pro Asp Pro Cys His  
565 570 575

Tyr Gly Ser Cys Lys Asp Gly Val Ala Thr Phe Thr Cys Leu Cys Arg  
580 585 590

Pro Gly Tyr Thr Gly His His Cys Glu Thr Asn Ile Asn Glu Cys Ser  
595 600 605

Ser Gln Pro Cys Arg Leu Arg Gly Thr Cys Gln Asp Pro Asp Asn Ala  
610 615 620

Tyr Leu Cys Phe Cys Leu Lys Gly Thr Thr Gly Pro Asn Cys Glu Ile  
625 630 635 640

Asn Leu Asp Asp Cys Ala Ser Ser Pro Cys Asp Ser Gly Thr Cys Leu  
645 650 655

Asp Lys Ile Asp Gly Tyr Glu Cys Ala Cys Glu Pro Gly Tyr Thr Gly  
660 665 670

Ser Met Cys Asn Ser Asn Ile Asp Glu Cys Ala Gly Asn Pro Cys His  
675 680 685

Asn Gly Gly Thr Cys Glu Asp Gly Ile Asn Gly Phe Thr Cys Arg Cys  
690 695 700

Pro Glu Gly Tyr His Asp Pro Thr Cys Leu Ser Glu Val Asn Glu Cys  
705 710 715 720

Asn Ser Asn Pro Cys Val His Gly Ala Cys Arg Asp Ser Leu Asn Gly  
725 730 735

Tyr Lys Cys Asp Cys Asp Pro Gly Trp Ser Gly Thr Asn Cys Asp Ile  
740 745 750

Asn Asn Asn Glu Cys Glu Ser Asn Pro Cys Val Asn Gly Gly Thr Cys  
755 760 765

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Lys Asp Met Thr Ser Gly Ile Val Cys Thr Cys Arg Glu Gly Phe Ser  
770 775 780

Gly Pro Asn Cys Gln Thr Asn Ile Asn Glu Cys Ala Ser Asn Pro Cys  
785 790 795 800

Leu Asn Lys Gly Thr Cys Ile Asp Asp Val Ala Gly Tyr Lys Cys Asn  
805 810 815

Cys Leu Leu Pro Tyr Thr Gly Ala Thr Cys Glu Val Val Leu Ala Pro  
820 825 830

Cys Ala Pro Ser Pro Cys Arg Asn Gly Gly Glu Cys Arg Gln Ser Glu  
835 840 845

Asp Tyr Glu Ser Phe Ser Cys Val Cys Pro Thr Ala Gly Ala Lys Gly  
850 855 860

Gln Thr Cys Glu Val Asp Ile Asn Glu Cys Val Leu Ser Pro Cys Arg  
865 870 875 880

His Gly Ala Ser Cys Gln Asn Thr His Gly Xaa Tyr Arg Cys His Cys  
885 890 895

Gln Ala Gly Tyr Ser Gly Arg Asn Cys Glu Thr Asp Ile Asp Asp Cys  
900 905 910

Arg Pro Asn Pro Cys His Asn Gly Gly Ser Cys Thr Asp Gly Ile Asn  
915 920 925

Thr Ala Phe Cys Asp Cys Leu Pro Gly Phe Arg Gly Thr Phe Cys Glu  
930 935 940

Glu Asp Ile Asn Glu Cys Ala Ser Asp Pro Cys Arg Asn Gly Ala Asn  
945 950 955 960

Cys Thr Asp Cys Val Asp Ser Tyr Thr Cys Thr Cys Pro Ala Gly Phe  
965 970 975

Ser Gly Ile His Cys Glu Asn Asn Thr Pro Asp Cys Thr Glu Ser Ser  
980 985 990

Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser Phe Thr Cys  
995 1000 1005

Leu Cys Pro Pro Gly Phe Thr Gly Ser Tyr Cys Gln His Val Val  
1010 1015 1020

Asn Glu Cys Asp Ser Arg Pro Cys Leu Leu Gly Gly Thr Cys Gln  
1025 1030 1035

## 212583.ST25

Asp Gly Arg Gly Leu His Arg 1040 Cys Thr Cys Pro Gln 1050 Gly Tyr Thr  
 1045  
 Gly Pro Asn Cys Gln Asn Leu Val His Trp Cys Asp 1065 Ser Ser Pro  
 1055 1060  
 Cys Lys Asn Gly Gly Lys Cys 1070 Trp Gln Thr His Thr 1080 Gln Tyr Arg  
 1075  
 Cys Glu Cys Pro Ser Gly 1085 Trp 1090 Thr Gly Leu Tyr Cys Asp Val Pro  
 1095  
 Ser Val Ser Cys Glu Val Ala 1100 Ala Gln Arg Gln Gly Val Asp Val  
 1105 1110  
 Ala Arg Leu Cys Gln His Gly 1115 1120 Gly Leu Cys Val Asp Ala Gly Asn  
 1125  
 Thr His His Cys Arg Cys Gln 1130 1135 Ala Gly Tyr Thr Gly Ser Tyr Cys  
 1140  
 Glu Asp Leu Val Asp Glu Cys 1145 1150 Ser Pro Ser Pro Cys Gln Asn Gly  
 1155  
 Ala Thr Cys Thr Asp Tyr Leu 1160 1165 Gly Gly Tyr Ser Cys Lys Cys Val  
 1170  
 Ala Gly Tyr His Gly Val Asn 1175 1180 Cys Ser Glu Glu Ile Asp Glu Cys  
 1185  
 Leu Ser His Pro Cys Gln Asn 1190 1195 Gly Gly Thr Cys Leu Asp Leu Pro  
 1200  
 Asn Thr Tyr Lys Cys Ser Cys 1205 1210 Pro Arg Gly Thr Gln Gly Val His  
 1215  
 Cys Glu Ile Asn Val Asp Asp 1220 1225 Cys Asn Pro Pro Val Asp Pro Val  
 1230  
 Ser Arg Ser Pro Lys Cys Phe 1235 1240 Asn Asn Gly Thr Cys Val Asp Gln  
 1245  
 Val Gly Gly Tyr Ser Cys Thr 1250 1255 Cys Pro Pro Gly Phe Val Gly Glu  
 1260  
 Arg Cys Glu Gly Asp Val Asn 1265 1270 Glu Cys Leu Ser Asn Pro Cys Asp  
 1275  
 Ala Arg Gly Thr Gln Asn Cys 1280 1285 Val Gln Arg Val Asn Asp Phe His  
 1290

## 212583.ST25

Cys Glu Cys Arg Ala Gly His Thr Gly Arg Arg Cys Glu Ser Val  
 1295 1300 1305  
 Ile Asn Gly Cys Lys Gly Lys Pro Cys Lys Asn Gly Gly Thr Cys  
 1310 1315 1320  
 Ala Val Ala Ser Asn Thr Ala Arg Gly Phe Ile Cys Lys Cys Pro  
 1325 1330 1335  
 Ala Gly Phe Glu Gly Ala Thr Cys Glu Asn Asp Ala Arg Thr Cys  
 1340 1345 1350  
 Gly Ser Leu Arg Cys Leu Asn Gly Gly Thr Cys Ile Ser Gly Pro  
 1355 1360 1365  
 Arg Ser Pro Thr Cys Leu Cys Leu Gly Pro Phe Thr Gly Pro Glu  
 1370 1375 1380  
 Cys Gln Phe Pro Ala Ser Ser Pro Cys Leu Gly Gly Asn Pro Cys  
 1385 1390 1395  
 Tyr Asn Gln Gly Thr Cys Glu Pro Thr Ser Glu Ser Pro Phe Tyr  
 1400 1405 1410  
 Arg Cys Leu Cys Pro Ala Lys Phe Asn Gly Leu Leu Cys His Ile  
 1415 1420 1425  
 Leu Asp Tyr Ser Phe Gly Gly Ala Gly Arg Asp Ile Pro Pro  
 1430 1435 1440  
 Pro Leu Ile Glu Glu Ala Cys Glu Leu Pro Glu Cys Gln Glu Asp  
 1445 1450 1455  
 Ala Gly Asn Lys Val Cys Ser Leu Gln Cys Asn Asn His Ala Cys  
 1460 1465 1470  
 Gly Trp Asp Gly Gly Asp Cys Ser Leu Asn Phe Asn Asp Pro Trp  
 1475 1480 1485  
 Lys Asn Cys Thr Gln Ser Leu Gln Cys Trp Lys Tyr Phe Ser Asp  
 1490 1495 1500  
 Gly His Cys Asp Ser Gln Cys Asn Ser Ala Gly Cys Leu Phe Asp  
 1505 1510 1515  
 Gly Phe Asp Cys Gln Arg Ala Glu Gly Gln Cys Asn Pro Leu Tyr  
 1520 1525 1530  
 Asp Gln Tyr Cys Lys Asp His Phe Ser Asp Gly His Cys Asp Gln  
 1535 1540 1545

## 212583.ST25

Gly Cys Asn Ser Ala Glu Cys Glu Trp Asp Gly Leu Asp Cys Ala  
 1550 1555 1560

Glu His Val Pro Glu Arg Leu Ala Ala Gly Thr Leu Val Val Val  
 1565 1570 1575

Val Leu Met Pro Pro Glu Gln Leu Arg Asn Ser Ser Phe His Phe  
 1580 1585 1590

Leu Arg Glu Leu Ser Arg Val Leu His Thr Asn Val Val Phe Lys  
 1595 1600 1605

Arg Asp Ala His Gly Gln Gln Met Ile Phe Pro Tyr Tyr Gly Arg  
 1610 1615 1620

Glu Glu Glu Leu Arg Lys His Pro Ile Lys Arg Ala Ala Glu Gly  
 1625 1630 1635

Trp Ala Ala Pro Asp Ala Leu Leu Gly Gln Val Lys Ala Ser Leu  
 1640 1645 1650

Leu Pro Gly Gly Ser Glu Gly Gly Arg Arg Arg Arg Glu Leu Asp  
 1655 1660 1665

Pro Met Asp Val Arg Gly Ser Ile Val Tyr Leu Glu Ile Asp Asn  
 1670 1675 1680

Arg Gln Cys Val Gln Ala Ser Ser Gln Cys Phe Gln Ser Ala Thr  
 1685 1690 1695

Asp Val Ala Ala Phe Leu Gly Ala Leu Ala Ser Leu Gly Ser Leu  
 1700 1705 1710

Asn Ile Pro Tyr Lys Ile Glu Ala Val Gln Ser Glu Thr Val Glu  
 1715 1720 1725

Pro Pro Pro Pro Ala Gln Leu His Phe Met Tyr Val Ala Ala Ala  
 1730 1735 1740

Ala Phe Val Leu Leu Phe Phe Val Gly Cys Gly Val Leu Leu Ser  
 1745 1750 1755

Arg Lys Arg Arg Xaa Gln His Gly Gln Leu Trp Phe Pro Glu Gly  
 1760 1765 1770

Phe Lys Val Ser Glu Ala Ser Lys Lys Lys Arg Arg Glu Xaa Leu  
 1775 1780 1785

Gly Glu Asp Ser Val Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp  
 1790 1795 1800

## 212583.ST25

Gly Ala Leu Met Asp Asp Asn Gln Asn Glu Trp Gly Asp Glu Asp  
 1805 1810 1815

Leu Glu Thr Lys Lys Phe Arg Phe Glu Glu Pro Val Val Leu Pro  
 1820 1825 1830

Asp Leu Asp Asp Gln Thr Asp His Arg Gln Trp Thr Gln Gln His  
 1835 1840 1845

Leu Asp Ala Ala Asp Leu Arg Met Ser Ala Met Ala Pro Thr Pro  
 1850 1855 1860

Pro Gln Gly Glu Val Asp Ala Asp Cys Met Asp Val Asn Val Arg  
 1865 1870 1875

Gly Pro Asp Gly Phe Thr Pro Leu Met Ile Ala Ser Cys Ser Gly  
 1880 1885 1890

Gly Gly Leu Glu Thr Gly Asn Ser Glu Glu Glu Glu Asp Ala Pro  
 1895 1900 1905

Ala Val Ile Ser Asp Phe Ile Tyr Gln Gly Ala Ser Leu His Asn  
 1910 1915 1920

Gln Thr Asp Arg Thr Gly Glu Thr Ala Leu His Leu Ala Ala Arg  
 1925 1930 1935

Tyr Ser Arg Ser Asp Ala Ala Lys Arg Leu Leu Glu Ala Ser Ala  
 1940 1945 1950

Asp Ala Asn Ile Gln Asp Asn Met Gly Arg Thr Pro Leu His Ala  
 1955 1960 1965

Ala Val Ser Ala Asp Ala Gln Gly Val Phe Gln Ile Leu Ile Arg  
 1970 1975 1980

Asn Arg Ala Thr Asp Leu Asp Ala Arg Met His Asp Gly Thr Thr  
 1985 1990 1995

Pro Leu Ile Leu Ala Ala Arg Leu Ala Val Glu Gly Met Leu Glu  
 2000 2005 2010

Asp Leu Ile Asn Ser His Ala Asp Val Asn Ala Val Asp Asp Leu  
 2015 2020 2025

Gly Lys Ser Ala Leu His Trp Ala Ala Ala Val Asn Asn Val Asp  
 2030 2035 2040

Ala Ala Val Val Leu Leu Lys Asn Gly Ala Asn Lys Asp Met Gln  
 2045 2050 2055

## 212583.ST25

Asn Asn Arg Glu Glu Thr Pro Leu Phe Leu Ala Ala Arg Glu Gly  
 2060 2065 2070

Ser Tyr Glu Thr Ala Lys Val Leu Leu Asp His Phe Ala Asn Arg  
 2075 2080 2085

Asp Ile Thr Asp His Met Asp Arg Leu Pro Arg Asp Ile Ala Gln  
 2090 2095 2100

Glu Arg Met His His Asp Ile Val Arg Leu Leu Asp Glu Tyr Asn  
 2105 2110 2115

Leu Val Arg Ser Pro Gln Leu His Gly Ala Pro Leu Gly Gly Thr  
 2120 2125 2130

Pro Thr Leu Ser Pro Pro Leu Cys Ser Pro Asn Gly Tyr Leu Gly  
 2135 2140 2145

Ser Leu Lys Pro Gly Val Gln Gly Lys Lys Val Arg Lys Pro Ser  
 2150 2155 2160

Ser Lys Gly Leu Ala Cys Gly Ser Lys Glu Ala Lys Asp Leu Lys  
 2165 2170 2175

Ala Arg Arg Lys Lys Ser Gln Asp Gly Lys Gly Cys Leu Leu Asp  
 2180 2185 2190

Ser Ser Gly Met Leu Ser Pro Val Asp Ser Leu Glu Ser Pro His  
 2195 2200 2205

Gly Tyr Leu Ser Asp Val Ala Ser Pro Pro Leu Leu Pro Ser Pro  
 2210 2215 2220

Phe Gln Gln Ser Pro Ser Val Pro Leu Asn His Leu Pro Gly Met  
 2225 2230 2235

Pro Asp Thr His Leu Gly Ile Gly His Leu Asn Val Ala Ala Lys  
 2240 2245 2250

Pro Glu Met Ala Ala Leu Gly Gly Gly Gly Arg Leu Ala Phe Glu  
 2255 2260 2265

Thr Gly Pro Pro Arg Leu Ser His Leu Pro Val Ala Ser Gly Thr  
 2270 2275 2280

Ser Thr Val Leu Gly Ser Ser Ser Gly Gly Ala Leu Asn Phe Thr  
 2285 2290 2295

Val Gly Gly Ser Thr Ser Leu Asn Gly Gln Cys Glu Trp Leu Ser  
 2300 2305 2310

## 212583.ST25

Arg Leu Gln Ser Gly Met Val Pro Asn Gln Tyr Asn Pro Leu Arg  
2315 2320 2325

Gly Ser Val Ala Pro Gly Pro Leu Ser Thr Gln Ala Pro Ser Leu  
2330 2335 2340

Gln His Gly Met Val Gly Pro Leu His Ser Ser Leu Ala Ala Ser  
2345 2350 2355

Ala Leu Ser Gln Met Met Ser Tyr Gln Gly Leu Pro Ser Thr Arg  
2360 2365 2370

Leu Ala Thr Gln Pro His Leu Val Gln Thr Gln Gln Val Gln Pro  
2375 2380 2385

Gln Asn Leu Gln Met Gln Gln Gln Asn Leu Gln Pro Ala Asn Ile  
2390 2395 2400

Gln Gln Gln Gln Ser Leu Gln Pro Pro Pro Pro Pro Gln Pro  
2405 2410 2415

His Leu Gly Val Ser Ser Ala Ala Ser Gly His Leu Gly Arg Ser  
2420 2425 2430

Phe Leu Ser Gly Glu Pro Ser Gln Ala Asp Val  
2435 2440

<210> 3

<211> 1218

<212> PRT

<213> Homo sapiens

<400> 3

Met Arg Ser Pro Arg Thr Arg Gly Arg Ser Gly Arg Pro Leu Ser Leu  
1 5 10 15

Leu Leu Ala Leu Leu Cys Ala Leu Arg Ala Lys Val Cys Gly Ala Ser  
20 25 30

Gly Gln Phe Glu Leu Glu Ile Leu Ser Met Gln Asn Val Asn Gly Glu  
35 40 45

Leu Gln Asn Gly Asn Cys Cys Gly Gly Ala Arg Asn Pro Gly Asp Arg  
50 55 60

Lys Cys Thr Arg Asp Glu Cys Asp Thr Tyr Phe Lys Val Cys Leu Lys  
65 70 75 80

## 212583.ST25

Glu Tyr Gln Ser Arg Val Thr Ala Gly Gly Pro Cys Ser Phe Gly Ser  
 85 90 95

Gly Ser Thr Pro Val Ile Gly Gly Asn Thr Phe Asn Leu Lys Ala Ser  
 100 105 110

Arg Gly Asn Asp Arg Asn Arg Ile Val Leu Pro Phe Ser Phe Ala Trp  
 115 120 125

Pro Arg Ser Tyr Thr Leu Leu Val Glu Ala Trp Asp Ser Ser Asn Asp  
 130 135 140

Thr Val Gln Pro Asp Ser Ile Ile Glu Lys Ala Ser His Ser Gly Met  
 145 150 155 160

Ile Asn Pro Ser Arg Gln Trp Gln Thr Leu Lys Gln Asn Thr Gly Val  
 165 170 175

Ala His Phe Glu Tyr Gln Ile Arg Val Thr Cys Asp Asp Tyr Tyr Tyr  
 180 185 190

Gly Phe Gly Cys Asn Lys Phe Cys Arg Pro Arg Asp Asp Phe Phe Gly  
 195 200 205

His Tyr Ala Cys Asp Gln Asn Gly Asn Lys Thr Cys Met Glu Gly Trp  
 210 215 220

Met Gly Pro Glu Cys Asn Arg Ala Ile Cys Arg Gln Gly Cys Ser Pro  
 225 230 235 240

Lys His Gly Ser Cys Lys Leu Pro Gly Asp Cys Arg Cys Gln Tyr Gly  
 245 250 255

Trp Gln Gly Leu Tyr Cys Asp Lys Cys Ile Pro His Pro Gly Cys Val  
 260 265 270

His Gly Ile Cys Asn Glu Pro Trp Gln Cys Leu Cys Glu Thr Asn Trp  
 275 280 285

Gly Gly Gln Leu Cys Asp Lys Asp Leu Asn Tyr Cys Gly Thr His Gln  
 290 295 300

Pro Cys Leu Asn Gly Gly Thr Cys Ser Asn Thr Gly Pro Asp Lys Tyr  
 305 310 315 320

Gln Cys Ser Cys Pro Glu Gly Tyr Ser Gly Pro Asn Cys Glu Ile Ala  
 325 330 335

Glu His Ala Cys Leu Ser Asp Pro Cys His Asn Arg Gly Ser Cys Lys  
 340 345 350

Glu Thr Ser Leu Gly Phe Glu Cys Glu Cys Ser Pro Gly Trp Thr Gly  
 355 360 365

Pro Thr Cys Ser Thr Asn Ile Asp Asp Cys Ser Pro Asn Asn Cys Ser  
 370 375 380

His Gly Gly Thr Cys Gln Asp Leu Val Asn Gly Phe Lys Cys Val Cys  
 385 390 395 400

Pro Pro Gln Trp Thr Gly Lys Thr Cys Gln Leu Asp Ala Asn Glu Cys  
 405 410 415

Glu Ala Lys Pro Cys Val Asn Ala Lys Ser Cys Lys Asn Leu Ile Ala  
 420 425 430

Ser Tyr Tyr Cys Asp Cys Leu Pro Gly Trp Met Gly Gln Asn Cys Asp  
 435 440 445

Ile Asn Ile Asn Asp Cys Leu Gly Gln Cys Gln Asn Asp Ala Ser Cys  
 450 455 460

Arg Asp Leu Val Asn Gly Tyr Arg Cys Ile Cys Pro Pro Gly Tyr Ala  
 465 470 475 480

Gly Asp His Cys Glu Arg Asp Ile Asp Glu Cys Ala Ser Asn Pro Cys  
 485 490 495

Leu Asn Gly Gly His Cys Gln Asn Glu Ile Asn Arg Phe Gln Cys Leu  
 500 505 510

Cys Pro Thr Gly Phe Ser Gly Asn Leu Cys Gln Leu Asp Ile Asp Tyr  
 515 520 525

Cys Glu Pro Asn Pro Cys Gln Asn Gly Ala Gln Cys Tyr Asn Arg Ala  
 530 535 540

Ser Asp Tyr Phe Cys Lys Cys Pro Glu Asp Tyr Glu Gly Lys Asn Cys  
 545 550 555 560

Ser His Leu Lys Asp His Cys Arg Thr Thr Pro Cys Glu Val Ile Asp  
 565 570 575

Ser Cys Thr Val Ala Met Ala Ser Asn Asp Thr Pro Glu Gly Val Arg  
 580 585 590

Tyr Ile Ser Ser Asn Val Cys Gly Pro His Gly Lys Cys Lys Ser Gln  
 595 600 605

Ser Gly Gly Lys Phe Thr Cys Asp Cys Asn Lys Gly Phe Thr Gly Thr  
 610 615 620

## 212583.ST25

Tyr Cys His Glu Asn Ile Asn Asp Cys Glu Ser Asn Pro Cys Arg Asn  
625 630 635 640

Gly Gly Thr Cys Ile Asp Gly Val Asn Ser Tyr Lys Cys Ile Cys Ser  
645 650 655

Asp Gly Trp Glu Gly Ala Tyr Cys Glu Thr Asn Ile Asn Asp Cys Ser  
660 665 670

Gln Asn Pro Cys His Asn Gly Gly Thr Cys Arg Asp Leu Val Asn Asp  
675 680 685

Phe Tyr Cys Asp Cys Lys Asn Gly Trp Lys Gly Lys Thr Cys His Ser  
690 695 700

Arg Asp Ser Gln Cys Asp Glu Ala Thr Cys Asn Asn Gly Gly Thr Cys  
705 710 715 720

Tyr Asp Glu Gly Asp Ala Phe Lys Cys Met Cys Pro Gly Gly Trp Glu  
725 730 735

Gly Thr Thr Cys Asn Ile Ala Arg Asn Ser Ser Cys Leu Pro Asn Pro  
740 745 750

Cys His Asn Gly Gly Thr Cys Val Val Asn Gly Glu Ser Phe Thr Cys  
755 760 765

Val Cys Lys Glu Gly Trp Glu Gly Pro Ile Cys Ala Gln Asn Thr Asn  
770 775 780

Asp Cys Ser Pro His Pro Cys Tyr Asn Ser Gly Thr Cys Val Asp Gly  
785 790 795 800

Asp Asn Trp Tyr Arg Cys Glu Cys Ala Pro Gly Phe Ala Gly Pro Asp  
805 810 815

Cys Arg Ile Asn Ile Asn Glu Cys Gln Ser Ser Pro Cys Ala Phe Gly  
820 825 830

Ala Thr Cys Val Asp Glu Ile Asn Gly Tyr Arg Cys Val Cys Pro Pro  
835 840 845

Gly His Ser Gly Ala Lys Cys Gln Glu Val Ser Gly Arg Pro Cys Ile  
850 855 860

Thr Met Gly Ser Val Ile Pro Asp Gly Ala Lys Trp Asp Asp Asp Cys  
865 870 875 880

Asn Thr Cys Gln Cys Leu Asn Gly Arg Ile Ala Cys Ser Lys Val Trp  
885 890 895

## 212583.ST25

Cys Gly Pro Arg Pro Cys Leu Leu His Lys Gly His Ser Glu Cys Pro  
900 905 910

Ser Gly Gln Ser Cys Ile Pro Ile Leu Asp Asp Gln Cys Phe Val His  
915 920 925

Pro Cys Thr Gly Val Gly Glu Cys Arg Ser Ser Ser Leu Gln Pro Val  
930 935 940

Lys Thr Lys Cys Thr Ser Asp Ser Tyr Tyr Gln Asp Asn Cys Ala Asn  
945 950 955 960

Ile Thr Phe Thr Phe Asn Lys Glu Met Met Ser Pro Gly Leu Thr Thr  
965 970 975

Glu His Ile Cys Ser Glu Leu Arg Asn Leu Asn Ile Leu Lys Asn Val  
980 985 990

Ser Ala Glu Tyr Ser Ile Tyr Ile Ala Cys Glu Pro Ser Pro Ser Ala  
995 1000 1005

Asn Asn Glu Ile His Val Ala Ile Ser Ala Glu Asp Ile Arg Asp  
1010 1015 1020

Asp Gly Asn Pro Ile Lys Glu Ile Thr Asp Lys Ile Ile Asp Leu  
1025 1030 1035

Val Ser Lys Arg Asp Gly Asn Ser Ser Leu Ile Ala Ala Val Ala  
1040 1045 1050

Glu Val Arg Val Gln Arg Arg Pro Leu Lys Asn Arg Thr Asp Phe  
1055 1060 1065

Leu Val Pro Leu Leu Ser Ser Val Leu Thr Val Ala Trp Ile Cys  
1070 1075 1080

Cys Leu Val Thr Ala Phe Tyr Trp Cys Leu Arg Lys Arg Arg Lys  
1085 1090 1095

Pro Gly Ser His Thr His Ser Ala Ser Glu Asp Asn Thr Thr Asn  
1100 1105 1110

Asn Val Arg Glu Gln Leu Asn Gln Ile Lys Asn Pro Ile Glu Lys  
1115 1120 1125

His Gly Ala Asn Thr Val Pro Ile Lys Asp Tyr Glu Asn Lys Asn  
1130 1135 1140

Ser Lys Met Ser Lys Ile Arg Thr His Asn Ser Glu Val Glu Glu  
1145 1150 1155

## 212583.ST25

Asp Asp Met Asp Lys His Gln Gln Lys Ala Arg Phe Ala Lys Gln  
 1160 1165 1170

Pro Ala Tyr Thr Leu Val Asp Arg Glu Glu Lys Pro Pro Asn Gly  
 1175 1180 1185

Thr Pro Thr Lys His Pro Asn Trp Thr Asn Lys Gln Asp Asn Arg  
 1190 1195 1200

Asp Leu Glu Ser Ala Gln Ser Leu Asn Arg Met Glu Tyr Ile Val  
 1205 1210 1215

<210> 4

<211> 1238

<212> PRT

<213> Homo sapiens

<400> 4

Met Arg Ala Gln Gly Arg Gly Arg Leu Pro Arg Arg Leu Leu Leu  
 1 5 10 15

Leu Ala Leu Trp Val Gln Ala Ala Arg Pro Met Gly Tyr Phe Glu Leu  
 20 25 30

Gln Leu Ser Ala Leu Arg Asn Val Asn Gly Glu Leu Leu Ser Gly Ala  
 35 40 45

Cys Cys Asp Gly Asp Gly Arg Thr Thr Arg Ala Gly Gly Cys Gly His  
 50 55 60

Asp Glu Cys Asp Thr Tyr Val Arg Val Cys Leu Lys Glu Tyr Gln Ala  
 65 70 75 80

Lys Val Thr Pro Thr Gly Pro Cys Ser Tyr Gly His Gly Ala Thr Pro  
 85 90 95

Val Leu Gly Gly Asn Ser Phe Tyr Leu Pro Pro Ala Gly Ala Ala Gly  
 100 105 110

Asp Arg Ala Arg Ala Arg Ala Gly Gly Asp Gln Asp Pro Gly  
 115 120 125

Leu Val Val Ile Pro Phe Gln Phe Ala Trp Pro Arg Ser Phe Thr Leu  
 130 135 140

Ile Val Glu Ala Trp Asp Trp Asp Asn Asp Thr Thr Pro Asn Glu Glu  
 145 150 155 160

## 212583.ST25

Leu Leu Ile Glu Arg Val Ser His Ala Gly Met Ile Asn Pro Glu Asp  
 165 170 175

Arg Trp Lys Ser Leu His Phe Ser Gly His Val Ala His Leu Glu Leu  
 180 185 190

Gln Ile Arg Val Arg Cys Asp Glu Asn Tyr Tyr Ser Ala Thr Cys Asn  
 195 200 205

Lys Phe Cys Arg Pro Arg Asn Asp Phe Phe Gly His Tyr Thr Cys Asp  
 210 215 220

Gln Tyr Gly Asn Lys Ala Cys Met Asp Gly Trp Met Gly Lys Glu Cys  
 225 230 235 240

Lys Glu Ala Val Cys Lys Gln Gly Cys Asn Leu Leu His Gly Gly Cys  
 245 250 255

Thr Val Pro Gly Glu Cys Arg Cys Ser Tyr Gly Trp Gln Gly Arg Phe  
 260 265 270

Cys Asp Glu Cys Val Pro Tyr Pro Gly Cys Val His Gly Ser Cys Val  
 275 280 285

Glu Pro Trp Gln Cys Asn Cys Glu Thr Asn Trp Gly Gly Leu Leu Cys  
 290 295 300

Asp Lys Asp Leu Asn Tyr Cys Gly Ser His His Pro Cys Thr Asn Gly  
 305 310 315 320

Gly Thr Cys Ile Asn Ala Glu Pro Asp Gln Tyr Arg Cys Thr Cys Pro  
 325 330 335

Asp Gly Tyr Ser Gly Arg Asn Cys Glu Lys Ala Glu His Ala Cys Thr  
 340 345 350

Ser Asn Pro Cys Ala Asn Gly Gly Ser Cys His Glu Val Pro Ser Gly  
 355 360 365

Phe Glu Cys His Cys Pro Ser Gly Trp Ser Gly Pro Thr Cys Ala Leu  
 370 375 380

Asp Ile Asp Glu Cys Ala Ser Asn Pro Cys Ala Ala Gly Gly Thr Cys  
 385 390 395 400

Val Asp Gln Val Asp Gly Phe Glu Cys Ile Cys Pro Glu Gln Trp Val  
 405 410 415

Gly Ala Thr Cys Gln Leu Asp Ala Asn Glu Cys Glu Gly Lys Pro Cys  
 420 425 430

## 212583.ST25

Leu Asn Ala Phe Ser Cys Lys Asn Leu Ile Gly Gly Tyr Tyr Cys Asp  
435 440 445

Cys Ile Pro Gly Trp Lys Gly Ile Asn Cys His Ile Asn Val Asn Asp  
450 455 460

Cys Arg Gly Gln Cys Gln His Gly Gly Thr Cys Lys Asp Leu Val Asn  
465 470 475 480

Gly Tyr Gln Cys Val Cys Pro Arg Gly Phe Gly Gly Arg His Cys Glu  
485 490 495

Leu Glu Arg Asp Lys Cys Ala Ser Ser Pro Cys His Ser Gly Gly Leu  
500 505 510

Cys Glu Asp Leu Ala Asp Gly Phe His Cys His Cys Pro Gln Gly Phe  
515 520 525

Ser Gly Pro Leu Cys Glu Val Asp Val Asp Leu Cys Glu Pro Ser Pro  
530 535 540

Cys Arg Asn Gly Ala Arg Cys Tyr Asn Leu Glu Gly Asp Tyr Tyr Cys  
545 550 555 560

Ala Cys Pro Asp Asp Phe Gly Gly Lys Asn Cys Ser Val Pro Arg Glu  
565 570 575

Pro Cys Pro Gly Gly Ala Cys Arg Val Ile Asp Gly Cys Gly Ser Asp  
580 585 590

Ala Gly Pro Gly Met Pro Gly Thr Ala Ala Ser Gly Val Cys Gly Pro  
595 600 605

His Gly Arg Cys Val Ser Gln Pro Gly Gly Asn Phe Ser Cys Ile Cys  
610 615 620

Asp Ser Gly Phe Thr Gly Thr Tyr Cys His Glu Asn Ile Asp Asp Cys  
625 630 635 640

Leu Gly Gln Pro Cys Arg Asn Gly Gly Thr Cys Ile Asp Glu Val Asp  
645 650 655

Ala Phe Arg Cys Phe Cys Pro Ser Gly Trp Glu Gly Glu Leu Cys Asp  
660 665 670

Thr Asn Pro Asn Asp Cys Leu Pro Asp Pro Cys His Ser Arg Gly Arg  
675 680 685

Cys Tyr Asp Leu Val Asn Asp Phe Tyr Cys Ala Cys Asp Asp Gly Trp  
690 695 700

## 212583.ST25

Lys Gly Lys Thr Cys His Ser Arg Glu Phe Gln Cys Asp Ala Tyr Thr  
705 710 715 720

Cys Ser Asn Gly Gly Thr Cys Tyr Asp Ser Gly Asp Thr Phe Arg Cys  
725 730 735

Ala Cys Pro Pro Gly Trp Lys Gly Ser Thr Cys Ala Val Ala Lys Asn  
740 745 750

Ser Ser Cys Leu Pro Asn Pro Cys Val Asn Gly Gly Thr Cys Val Gly  
755 760 765

Ser Gly Ala Ser Phe Ser Cys Ile Cys Arg Asp Gly Trp Glu Gly Arg  
770 775 780

Thr Cys Thr His Asn Thr Asn Asp Cys Asn Pro Leu Pro Cys Tyr Asn  
785 790 795 800

Gly Gly Ile Cys Val Asp Gly Val Asn Trp Phe Arg Cys Glu Cys Ala  
805 810 815

Pro Gly Phe Ala Gly Pro Asp Cys Arg Ile Asn Ile Asp Glu Cys Gln  
820 825 830

Ser Ser Pro Cys Ala Tyr Gly Ala Thr Cys Val Asp Glu Ile Asn Gly  
835 840 845

Tyr Arg Cys Ser Cys Pro Pro Gly Arg Ala Gly Pro Arg Cys Gln Glu  
850 855 860

Val Ile Gly Phe Gly Arg Ser Cys Trp Ser Arg Gly Thr Pro Phe Pro  
865 870 875 880

His Gly Ser Ser Trp Val Glu Asp Cys Asn Ser Cys Arg Cys Leu Asp  
885 890 895

Gly Arg Arg Asp Cys Ser Lys Val Trp Cys Gly Trp Lys Pro Cys Leu  
900 905 910

Leu Ala Gly Gln Pro Glu Ala Leu Ser Ala Gln Cys Pro Leu Gly Gln  
915 920 925

Arg Cys Leu Glu Lys Ala Pro Gly Gln Cys Leu Arg Pro Pro Cys Glu  
930 935 940

Ala Trp Gly Glu Cys Gly Ala Glu Glu Pro Pro Ser Thr Pro Cys Leu  
945 950 955 960

Pro Arg Ser Gly His Leu Asp Asn Asn Cys Ala Arg Leu Thr Leu His  
965 970 975

## 212583.ST25

Phe Asn Arg Asp His Val Pro Gln Gly Thr Thr Val Gly Ala Ile Cys  
 980 985 990  
 Ser Gly Ile Arg Ser Leu Pro Ala Thr Arg Ala Val Ala Arg Asp Arg  
 995 1000 1005  
 Leu Leu Val Leu Leu Cys Asp Arg Ala Ser Ser Gly Ala Ser Ala  
 1010 1015 1020  
 Val Glu Val Ala Val Ser Phe Ser Pro Ala Arg Asp Leu Pro Asp  
 1025 1030 1035  
 Ser Ser Leu Ile Gln Gly Ala Ala His Ala Ile Val Ala Ala Ile  
 1040 1045 1050  
 Thr Gln Arg Gly Asn Ser Ser Leu Leu Leu Ala Val Thr Glu Val  
 1055 1060 1065  
 Lys Val Glu Thr Val Val Thr Gly Gly Ser Ser Thr Gly Leu Leu  
 1070 1075 1080  
 Val Pro Val Leu Cys Gly Ala Phe Ser Val Leu Trp Leu Ala Cys  
 1085 1090 1095  
 Val Val Leu Cys Val Trp Trp Thr Arg Lys Arg Arg Lys Glu Arg  
 1100 1105 1110  
 Glu Arg Ser Arg Leu Pro Arg Glu Glu Ser Ala Asn Asn Gln Trp  
 1115 1120 1125  
 Ala Pro Leu Asn Pro Ile Arg Asn Pro Ile Glu Arg Pro Gly Gly  
 1130 1135 1140  
 His Lys Asp Val Leu Tyr Gln Cys Lys Asn Phe Thr Pro Pro Pro  
 1145 1150 1155  
 Arg Arg Ala Asp Glu Ala Leu Pro Gly Pro Ala Gly His Ala Ala  
 1160 1165 1170  
 Val Arg Glu Asp Glu Glu Asp Glu Asp Leu Gly Arg Gly Glu Glu  
 1175 1180 1185  
 Asp Ser Leu Glu Ala Glu Lys Phe Leu Ser His Lys Phe Thr Lys  
 1190 1195 1200  
 Asp Pro Gly Arg Ser Pro Gly Arg Pro Ala His Trp Ala Ser Gly  
 1205 1210 1215  
 Pro Lys Val Asp Asn Arg Ala Val Arg Ser Ile Asn Glu Ala Arg  
 1220 1225 1230

Tyr Val Gly Lys Glu  
1235

<210> 5

<211> 257

<212> PRT

<213> Homo sapiens

<400> 5

Pro Leu Ala Glu Pro Leu Ala Pro Arg Asp Val Phe Ile Ala Val Lys  
1 5 10 15

Thr Thr Lys Lys Phe His Arg Ala Arg Leu Asp Leu Leu Leu Glu Thr  
20 25 30

Trp Ile Ser Arg His Lys Glu Met Thr Phe Ile Phe Thr Asp Gly Glu  
35 40 45

Asp Glu Ala Leu Ala Arg His Thr Gly Asn Val Val Ile Thr Asn Cys  
50 55 60

Ser Ala Ala His Ser Arg Gln Ala Leu Ser Cys Lys Met Ala Val Glu  
65 70 75 80

Tyr Asp Arg Phe Ile Glu Ser Gly Arg Lys Trp Phe Cys His Val Asp  
85 90 95

Asp Asp Asn Tyr Val Asn Leu Arg Ala Leu Leu Leu Leu Ala Ser  
100 105 110

Tyr Pro His Thr Leu Asp Val Tyr Val Gly Lys Pro Ser Leu Asp Arg  
115 120 125

Pro Ile Gln Ala Met Glu Arg Val Ser Glu Asn Lys Val Arg Pro Val  
130 135 140

His Phe Trp Phe Ala Thr Gly Gly Ala Gly Phe Cys Ile Ser Arg Gly  
145 150 155 160

Leu Ala Leu Lys Met Ser Pro Trp Ala Ser Gly Gly His Phe Met Asn  
165 170 175

Thr Ala Glu Arg Ile Arg Leu Pro Asp Asp Cys Thr Ile Gly Tyr Ile  
180 185 190

Val Glu Ala Leu Leu Gly Val Pro Leu Ile Arg Ser Gly Leu Phe His  
195 200 205

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Ser His Leu Glu Asn Leu Gln Gln Val Pro Thr Ser Glu Leu His Glu  
210 215 220

Gln Val Thr Leu Ser Tyr Gly Met Phe Glu Asn Lys Arg Asn Ala Val  
225 230 235 240

His Val Lys Gly Pro Phe Ser Val Glu Ala Asp Pro Ser Arg Trp Gly  
245 250 255

Asn

<210> 6

<211> 321

<212> PRT

<213> Homo sapiens

<400> 6

Met Gln Cys Arg Leu Pro Arg Gly Leu Ala Gly Ala Leu Leu Thr Leu  
1 5 10 15

Leu Cys Met Gly Leu Leu Cys Leu Arg Tyr His Leu Asn Leu Ser Pro  
20 25 30

Gln Arg Val Gln Gly Thr Pro Glu Leu Ser Gln Pro Asn Pro Gly Pro  
35 40 45

Pro Lys Leu Gln Leu His Asp Val Phe Ile Ala Val Lys Thr Thr Arg  
50 55 60

Ala Phe His Arg Leu Arg Leu Glu Leu Leu Leu Asp Thr Trp Val Ser  
65 70 75 80

Arg Thr Arg Glu Leu Thr Phe Val Phe Thr Asp Ser Pro Asp Lys Gly  
85 90 95

Leu Gln Glu Arg Leu Gly Ser His Leu Val Val Thr Asn Cys Ser Ala  
100 105 110

Glu His Ser His Pro Ala Leu Ser Cys Lys Met Ala Ala Glu Phe Asp  
115 120 125

Thr Phe Leu Ala Ser Gly Leu Arg Trp Phe Cys His Val Asp Asp Asp  
130 135 140

Asn Tyr Val Asn Pro Arg Ala Leu Leu Gln Leu Leu Arg Ala Phe Pro  
145 150 155 160

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Leu Ala Arg Asp Val Tyr Val Gly Arg Pro Ser Leu Asn Arg Pro Ile  
 165 170 175

His Ala Ser Glu Pro Gln Pro His Asn Arg Thr Arg Leu Val Gln Phe  
 180 185 190

Trp Phe Ala Thr Gly Gly Ala Gln Phe Cys Ile Asn Arg Lys Leu Ala  
 195 200 205

Leu Lys Met Ala Pro Trp Ala Ser Gly Ser Arg Phe Met Asp Thr Ser  
 210 215 220

Ala Leu Ile Arg Leu Pro Asp Asp Cys Thr Met Gly Tyr Ile Ile Glu  
 225 230 235 240

Cys Lys Leu Gly Gly Arg Leu Gln Pro Ser Pro Leu Phe His Ser His  
 245 250 255

Leu Glu Thr Leu Gln Leu Leu Arg Thr Ala Gln Leu Pro Glu Gln Val  
 260 265 270

Thr Leu Ser Tyr Gly Val Phe Glu Gly Lys Leu Asn Val Ile Lys Leu  
 275 280 285

Gln Gly Pro Phe Ser Pro Glu Glu Asp Pro Ser Arg Phe Arg Ser Leu  
 290 295 300

His Cys Leu Leu Tyr Pro Asp Thr Pro Trp Cys Pro Gln Leu Gly Ala  
 305 310 315 320

Arg

<210> 7

<211> 191

<212> PRT

<213> Homo sapiens

<400> 7

Met Ser Arg Ala Arg Gly Ala Leu Cys Arg Ala Cys Leu Ala Leu Ala  
 1 5 10 15

Ala Ala Leu Ala Ala Leu Leu Leu Pro Leu Pro Leu Pro Arg Ala  
 20 25 30

Pro Ala Pro Ala Arg Thr Pro Ala Pro Ala Pro Arg Ala Pro Pro Ser  
 35 40 45

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Arg Pro Ala Ala Pro Ser Leu Arg Pro Asp Asp Val Phe Ile Ala Val  
50 55 60

Lys Thr Thr Arg Lys Asn His Gly Pro Arg Leu Arg Leu Leu Leu Arg  
65 70 75 80

Thr Trp Ile Ser Arg Ala Arg Gln Gln Thr Phe Ile Phe Thr Asp Gly  
85 90 95

Asp Asp Pro Glu Leu Glu Leu Gln Gly Asp Arg Val Ile Asn Thr  
100 105 110

Asn Cys Ser Ala Val Arg Thr Arg Gln Ala Leu Cys Cys Lys Met Ser  
115 120 125

Val Glu Tyr Asp Lys Phe Ile Glu Ser Gly Arg Lys Trp Phe Cys His  
130 135 140

Val Asp Asp Asp Asn Tyr Val Asn Ala Arg Ser Leu Leu His Leu Leu  
145 150 155 160

Ser Ser Phe Ser Pro Ser Gln Asp Val Tyr Leu Gly Arg Pro Ser Leu  
165 170 175

Asp His Pro Ile Glu Ala Thr Glu Arg Val Gln Gly Gly Arg Thr  
180 185 190

<210> 8

<211> 1404

<212> PRT

<213> Drosophila melanogaster

<400> 8

Met Phe Arg Lys His Phe Arg Arg Lys Pro Ala Thr Ser Ser Leu  
1 5 10 15

Glu Ser Thr Ile Glu Ser Ala Asp Ser Leu Gly Met Ser Lys Lys Thr  
20 25 30

Ala Thr Lys Arg Gln Arg Pro Arg His Arg Val Pro Lys Ile Ala Thr  
35 40 45

Leu Pro Ser Thr Ile Arg Asp Cys Arg Ser Leu Lys Ser Ala Cys Asn  
50 55 60

Leu Ile Ala Leu Ile Leu Ile Leu Val His Lys Ile Ser Ala Ala  
65 70 75 80

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Gly Asn Phe Glu Leu Glu Ile Leu Glu Ile Ser Asn Thr Asn Ser His  
85 90 95

Leu Leu Asn Gly Tyr Cys Cys Gly Met Pro Ala Glu Leu Arg Ala Thr  
100 105 110

Lys Thr Ile Gly Cys Ser Pro Cys Thr Thr Ala Phe Arg Leu Cys Leu  
115 120 125

Lys Glu Tyr Gln Thr Thr Glu Gln Gly Ala Ser Ile Ser Thr Gly Cys  
130 135 140

Ser Phe Gly Asn Ala Thr Thr Lys Ile Leu Gly Gly Ser Ser Phe Val  
145 150 155 160

Leu Ser Asp Pro Gly Val Gly Ala Ile Val Leu Pro Phe Thr Phe Arg  
165 170 175

Trp Thr Lys Ser Phe Thr Leu Ile Leu Gln Ala Leu Asp Met Tyr Asn  
180 185 190

Thr Ser Tyr Pro Asp Ala Glu Arg Leu Ile Glu Glu Thr Ser Tyr Ser  
195 200 205

Gly Val Ile Leu Pro Ser Pro Glu Trp Lys Thr Leu Asp His Ile Gly  
210 215 220

Arg Asn Ala Arg Ile Thr Tyr Arg Val Arg Val Gln Cys Ala Val Thr  
225 230 235 240

Tyr Tyr Asn Thr Thr Cys Thr Thr Phe Cys Arg Pro Arg Asp Asp Gln  
245 250 255

Phe Gly His Tyr Ala Cys Gly Ser Glu Gly Gln Lys Leu Cys Leu Asn  
260 265 270

Gly Trp Gln Gly Val Asn Cys Glu Glu Ala Ile Cys Lys Ala Gly Cys  
275 280 285

Asp Pro Val His Gly Lys Cys Asp Arg Pro Gly Glu Cys Glu Cys Arg  
290 295 300

Pro Gly Trp Arg Gly Pro Leu Cys Asn Glu Cys Met Val Tyr Pro Gly  
305 310 315 320

Cys Lys His Gly Ser Cys Asn Gly Ser Ala Trp Lys Cys Val Cys Asp  
325 330 335

Thr Asn Trp Gly Gly Ile Leu Cys Asp Gln Asp Leu Asn Phe Cys Gly  
340 345 350

## 212583.ST25

Thr His Glu Pro Cys Lys His Gly Gly Thr Cys Glu Asn Thr Ala Pro  
355 360 365

Asp Lys Tyr Arg Cys Thr Cys Ala Glu Gly Leu Ser Gly Glu Gln Cys  
370 375 380

Glu Ile Val Glu His Pro Cys Ala Thr Arg Pro Cys Arg Asn Gly Gly  
385 390 395 400

Thr Cys Thr Leu Lys Thr Ser Asn Arg Thr Gln Ala Gln Val Tyr Arg  
405 410 415

Thr Ser His Gly Arg Ser Asn Met Gly Arg Pro Val Arg Arg Ser Ser  
420 425 430

Ser Met Arg Ser Leu Asp His Leu Arg Pro Glu Gly Gln Ala Leu Asn  
435 440 445

Gly Ser Ser Ser Ser Gly Leu Val Ser Leu Gly Ser Leu Gln Leu Gln  
450 455 460

Gln Gln Leu Ala Pro Asp Phe Thr Cys Asp Cys Ala Ala Gly Trp Thr  
465 470 475 480

Gly Pro Thr Cys Glu Ile Asn Ile Asp Glu Cys Ala Gly Gly Pro Cys  
485 490 495

Glu His Gly Thr Cys Ile Asp Leu Ile Gly Gly Phe Arg Cys Glu  
500 505 510

Cys Pro Pro Glu Trp His Gly Asp Val Cys Gln Val Asp Val Asn Glu  
515 520 525

Cys Glu Ala Pro His Ser Ala Gly Ile Ala Ala Asn Ala Leu Leu Thr  
530 535 540

Thr Thr Ala Thr Ala Ile Ile Gly Ser Asn Leu Ser Ser Thr Ala Leu  
545 550 555 560

Leu Ala Ala Leu Thr Ser Ala Val Ala Ser Thr Ser Leu Ala Ile Gly  
565 570 575

Pro Cys Ile Asn Ala Lys Glu Cys Arg Asn Gln Pro Gly Ser Phe Ala  
580 585 590

Cys Ile Cys Lys Glu Gly Trp Gly Gly Val Thr Cys Ala Glu Asn Leu  
595 600 605

Asp Asp Cys Val Gly Gln Cys Arg Asn Gly Ala Thr Cys Ile Asp Leu  
610 615 620

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val Asn Asp Tyr Arg Cys Ala Cys Ala Ser Gly Phe Thr Gly Arg Asp  
625 630 635 640

Cys Glu Thr Asp Ile Asp Glu Cys Ala Thr Ser Pro Cys Arg Asn Gly  
645 650 655

Gly Glu Cys val Asp Met Val Gly Lys Phe Asn Cys Ile Cys Pro Leu  
660 665 670

Gly Tyr Ser Gly Ser Leu Cys Glu Glu Ala Lys Glu Asn Cys Thr Pro  
675 680 685

Ser Pro Cys Leu Glu Gly His Cys Leu Asn Thr Pro Glu Gly Tyr Tyr  
690 695 700

Cys His Cys Pro Pro Asp Arg Ala Gly Lys His Cys Glu Gln Leu Arg  
705 710 715 720

Pro Leu Cys Ser Gln Pro Pro Cys Asn Glu Gly Cys Phe Ala Asn Val  
725 730 735

Ser Leu Ala Thr Ser Ala Thr Thr Thr Thr Thr Thr Thr Ala  
740 745 750

Thr Thr Thr Arg Lys Met Ala Lys Pro Ser Gly Leu Pro Cys Ser Gly  
755 760 765

His Gly Ser Cys Glu Met Ser Asp Val Gly Thr Phe Cys Lys Cys His  
770 775 780

Val Gly His Thr Gly Thr Phe Cys Glu His Asn Leu Asn Glu Cys Ser  
785 790 795 800

Pro Asn Pro Cys Arg Asn Gly Gly Ile Cys Leu Asp Gly Asp Gly Asp  
805 810 815

Phe Thr Cys Glu Cys Met Ser Gly Trp Thr Gly Lys Arg Cys Ser Glu  
820 825 830

Arg Ala Thr Gly Cys Tyr Ala Gly Gln Cys Gln Asn Gly Gly Thr Cys  
835 840 845

Met Pro Gly Ala Pro Asp Lys Ala Leu Gln Pro His Cys Arg Cys Ala  
850 855 860

Pro Gly Trp Thr Gly Leu Phe Cys Ala Glu Ala Ile Asp Gln Cys Arg  
865 870 875 880

Gly Gln Pro Cys His Asn Gly Gly Thr Cys Glu Ser Gly Ala Gly Trp  
885 890 895

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Phe Arg Cys Val Cys Ala Gln Gly Phe Ser Gly Pro Asp Cys Arg Ile  
900 905 910

Ash Val Ashn Glu Cys Ser Pro Gln Pro Cys Gln Gly Gly Ala Thr Cys  
915 920 925

Ile Asp Gly Ile Gly Gly Tyr Ser Cys Ile Cys Pro Pro Gly Arg His  
930 935 940

Gly Leu Arg Cys Glu Ile Leu Leu Ser Asp Pro Lys Ser Ala Cys Gln  
945 950 955 960

Asn Ala Ser Asn Thr Ile Ser Pro Tyr Thr Ala Leu Asn Arg Ser Gln  
965 970 975

Asn Trp Leu Asp Ile Ala Leu Thr Gly Arg Thr Glu Asp Asp Glu Asn  
980 985 990

Cys Asn Ala Cys Val Cys Glu Asn Gly Thr Ser Arg Cys Thr Asn Leu  
995 1000 1005

Trp Cys Gly Leu Pro Asn Cys Tyr Lys Val Asp Pro Leu Ser Lys  
1010 1015 1020

Ser Ser Asn Leu Ser Gly Val Cys Lys Gln His Glu Val Cys Val  
1025 1030 1035

Pro Ala Leu Ser Glu Thr Cys Leu Ser Ser Pro Cys Asn Val Arg  
1040 1045 1050

Gly Asp Cys Arg Ala Leu Glu Pro Ser Arg Arg Val Ala Pro Pro  
1055 1060 1065

Arg Leu Pro Ala Lys Ser Ser Cys Trp Pro Asn Gln Ala Val Val  
1070 1075 1080

Asn Glu Asn Cys Ala Arg Leu Thr Ile Leu Leu Ala Leu Glu Arg  
1085 1090 1095

Val Gly Lys Gly Ala Ser Val Glu Gly Leu Cys Ser Leu Val Arg  
1100 1105 1110

Val Leu Leu Ala Ala Gln Leu Ile Lys Lys Pro Ala Ser Thr Phe  
1115 1120 1125

Gly Gln Asp Pro Gly Met Leu Met Val Leu Cys Asp Leu Lys Thr  
1130 1135 1140

Gly Thr Asn Asp Thr Val Glu Leu Thr Val Ser Ser Ser Lys Leu  
1145 1150 1155

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Asn Asp Pro Gln Leu Pro Val Ala Val Gly Leu Leu Gly Glu Leu  
 1160 1165 1170

Leu Ser Ser Arg Gln Leu Asn Gly Ile Gln Arg Arg Lys Glu Leu  
 1175 1180 1185

Glu Leu Gln His Ala Lys Leu Ala Ala Leu Thr Ser Ile Val Glu  
 1190 1195 1200

Val Lys Leu Glu Thr Ala Arg Val Ala Asp Gly Ser Gly His Ser  
 1205 1210 1215

Leu Leu Ile Gly Val Leu Cys Gly Val Phe Ile Val Leu Val Gly  
 1220 1225 1230

Phe Ser Val Phe Ile Ser Leu Tyr Trp Lys Gln Arg Leu Ala Tyr  
 1235 1240 1245

Arg Thr Ser Ser Gly Met Asn Leu Thr Pro Ser Leu Asp Ala Leu  
 1250 1255 1260

Arg His Glu Glu Glu Lys Ser Asn Asn Leu Gln Asn Glu Glu Asn  
 1265 1270 1275

Leu Arg Arg Tyr Thr Asn Pro Leu Lys Gly Ser Thr Ser Ser Leu  
 1280 1285 1290

Arg Ala Ala Thr Gly Met Glu Leu Ser Leu Asn Pro Ala Pro Glu  
 1295 1300 1305

Leu Ala Ala Ser Ala Ala Ser Ser Ser Ala Leu His Arg Ser Gln  
 1310 1315 1320

Pro Leu Phe Pro Pro Cys Asp Phe Glu Arg Glu Leu Asp Ser Ser  
 1325 1330 1335

Thr Gly Leu Lys Gln Ala His Lys Arg Ser Ser Gln Ile Leu Leu  
 1340 1345 1350

His Lys Thr Gln Asn Ser Asp Met Arg Lys Asn Thr Val Gly Ser  
 1355 1360 1365

Leu Asp Ser Pro Arg Lys Asp Phe Gly Lys Arg Ser Ile Asn Cys  
 1370 1375 1380

Lys Ser Met Pro Pro Ser Ser Gly Asp Glu Gly Ser Asp Val Leu  
 1385 1390 1395

Ala Thr Thr Val Met Val  
 1400

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<210> 9  
<211> 17  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> JAG-1b Notch ligand  
<220>  
<221> misc\_feature  
<223> JAG-1c Notch ligand

<400> 9  
Ala Asp Asp Tyr Tyr Tyr Gly Phe Gly Ala Asn Lys Phe Gly Arg Pro  
1 5 10 15

Arg

<210> 10  
<211> 21  
<212> PRT  
<213> artificial/unknown

<220>  
<221> misc\_feature  
<223> JAG-1c Notch ligand

<400> 10  
Ala Asp Asp Tyr Tyr Tyr Gly Phe Gly Ala Asn Lys Phe Gly Arg Pro  
1 5 10 15

Arg Asp Asp Phe Phe  
20

<210> 11  
<211> 17  
<212> PRT  
<213> artificial/unknown

<220>  
<221> misc\_feature  
<223> JAG-1 Notch ligand

<400> 11

Cys Asp Asp Tyr Tyr Gly Phe Gly Cys Asn Lys Phe Cys Arg Pro  
1 5 10 15

Arg

<210> 12  
<211> 19  
<212> PRT  
<213> artificial/unknown

<220>  
<221> misc\_feature  
<223> r-JAG1 Notch ligand

<400> 12

Cys Asp Asp Tyr Tyr Gly Phe Gly Cys Asn Lys Phe Gly Arg Pro  
1 5 10 15

Arg Asp Asp

<210> 13  
<211> 17  
<212> PRT  
<213> artificial/unknown

<220>  
<221> misc\_feature  
<223> Scrambled JAG peptide

<400> 13

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Arg Cys Gly Pro Asp Cys Phe Asp Asn Tyr Gly Arg Tyr Lys Tyr Cys  
1 5 10 15

Phe

<210> 14

<211> 22

<212> DNA

<213> artificial/unknown

<220>

<221> misc\_feature

<223> NF kappa B oligonucleotide

<400> 14

agttgagggg actttccag gc

22

<210> 15

<211> 282

<212> DNA

<213> Artificial/Unknown

<220>

<221> misc\_feature

<223> Human Notch repeats 11-12 - a Notch antagonistic polypeptide

<220>

<221> exon

<222> (1)..(282)

<223>

<220>

<221> misc\_feature

<222> (1)..(33)

<223> encodes a tag that is dispensable for Notch antagonistic activity

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<400> 15		
atg gct gca gaa ttc cat cat cat cat cat cat cag gac gtg gat gag	48	
Met Ala Ala Glu Phe His His His His His Gln Asp Val Asp Glu		
1 5 10 15		
tgc tcg ctg ggt gcc aac ccc tgc gag cat gcg ggc aag tgc atc aac	96	
Cys Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn		
20 25 30		
acg ctg ggc tcc ttc gag tgc cag tgt ctg cag ggc tac acg ggc ccc	144	
Thr Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro		
35 40 45		
cga tgc gag atc gac gtc aac gag tgc gtc tcg aac ccg tgc cag aac	192	
Arg Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn		
50 55 60		
gac gcc acc tgc ctg gac cag att ggg gag ttc cag tgc atg tgc atg	240	
Asp Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Met Cys Met		
65 70 75 80		
ccc ggc tac gag ggt gtg cac tgc gag gtc aac aca tga tga	282	
Pro Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr		
85 90		

<210> 16

<211> 92

<212> PRT

<213> Artificial/Unknown

<220>

<221> Misc

<222> (1)..(92)

<223> Notch antagonist polypeptide containing tag sequence

<220>

<221> Misc

<222> (1)..(11)

<223> tag sequence for detecting polypeptide

<220>

<221> Misc

<222> (12)..(92)

<223> human Notch repeats 11 and 12

<400> 16

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Met Ala Ala Glu Phe His His His His His Gln Asp Val Asp Glu  
 1 5 10 15

Cys Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn  
 20 25 30

Thr Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro  
 35 40 45

Arg Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn  
 50 55 60

Asp Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Met Cys Met  
 65 70 75 80

Pro Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr  
 85 90

<210> 17

<211> 249

<212> DNA

<213> Artificial/Unknown

<220>

<221> exon

<222> (1)..(249)

<223> Encodes human Notch repeats 11-12

<400> 17  
 cag gac gtg gat gag tgc tcg ctg ggt gcc aac ccc tgc gag cat gcg 48  
 Gln Asp Val Asp Glu Cys Ser Leu Gly Ala Asn Pro Cys Glu His Ala  
 1 5 10 15

ggc aag tgc atc aac acg ctg ggc tcc ttc gag tgc cag tgt ctg cag 96  
 Gly Lys Cys Ile Asn Thr Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln  
 20 25 30

ggc tac acg ggc ccc cga tgc gag atc gac gtc aac gag tgc gtc tcg 144  
 Gly Tyr Thr Gly Pro Arg Cys Glu Ile Asp Val Asn Glu Cys Val Ser  
 35 40 45

aac ccg tgc cag aac gac gcc acc tgc ctg gac cag att ggg gag ttc 192  
 Asn Pro Cys Gln Asn Asp Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe  
 50 55 60

cag tgc atg tgc atg ccc ggc tac gag ggt gtg cac tgc gag gtc aac 240  
 Gln Cys Met Cys Met Pro Gly Tyr Glu Gly Val His Cys Glu Val Asn  
 65 70 75 80

aca tga tga  
 Thr 249

<210> 18  
<211> 81  
<212> PRT  
<213> Artificial/unknown

<220>  
<221> misc  
<222> (1)..(81)  
<223> Human Notch repeats 11 and 12 - functions as Notch antagonist

<400> 18

Gln Asp Val Asp Glu Cys Ser Leu Gly Ala Asn Pro Cys Glu His Ala  
1 5 10 15

Gly Lys Cys Ile Asn Thr Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln  
20 25 30

Gly Tyr Thr Gly Pro Arg Cys Glu Ile Asp Val Asn Glu Cys Val Ser  
35 40 45

Asn Pro Cys Gln Asn Asp Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe  
50 55 60

Gln Cys Met Cys Met Pro Gly Tyr Glu Gly Val His Cys Glu Val Asn  
65 70 75 80

Thr